Practice pointer: covid-19 antibody testing

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Box 1: What you need to know

- Positive antibodies demonstrate evidence of prior exposure to SARS-CoV-2 virus
- Antibody testing should be undertaken at least 2 weeks after symptom onset
- The sensitivity and specificity of antibody tests varies over time and results should be interpreted in context of the clinical history
- Antibody testing could have a useful role in covid-19 diagnosis in patients with late presentation, prolonged symptoms or negative RT-PCR tests
- For most asymptomatic individuals, knowing their antibody status is unlikely to change clinical management

Background

The covid-19 pandemic represents a significant challenge to clinicians, to healthcare systems and to public health globally. Diagnosis can be challenging as symptoms can vary significantly, and false negative RT-PCR tests occur,[1] particularly when swabs are done more than 5 days after symptom onset, when sensitivity of RT-PCR tests starts to decrease.[2] A significant proportion of infections may also be asymptomatic,[3] and many in the UK who have had COVID-19 symptoms isolated at home without ever being tested. The emotional strain of the current pandemic is significant, leading to fear and a desire for reassurance and certainty. Consequently there has been substantial interest in antibody testing, both to measure how far the infection has spread and to identify individuals who have antibodies, as lockdowns are gradually lifted.[4] Despite a rapidly increasing number of research papers, there is a lack of clarity about how these tests fit into clinical pathways, and how to interpret results. The UK government has announced that antibody testing should be offered to anyone having their blood taken who wants to know whether they have been infected with covid-19, even if there is '*not a specific clinical indication*',[5] yet currently there is no clear guidance for clinicians on how to interpret these results to make optimal decisions for individual patients. The UK are soon to introduce the UK-Rapid Test Consortium "AbC-19™ Rapid Test" and promise that it will be widely

available to the public. (https://www.abingdonhealth.com/uk-covid-19-rapid-antibody-tests-approved-for-professional-use/)

Who might benefit from antibody testing?

There are four main possible reasons for covid-19 antibody testing;

1) For diagnosis of individuals with current symptoms suggestive of covid-19, when antigen testing has failed to detect SARS-CoV-2, especially those who present two weeks or more after symptom onset (when antibody testing becomes more reliable).
2) For individuals who are currently asymptomatic, to assess if they have had a previous SARS-CoV-2 infection. This may include people at higher risk of severe disease eg BAME groups or those with occupational risk of infection eg healthcare workers, in order to provide reassurance, or to inform personal decisions about returning to work.
3) To monitor the quality and longevity of the immune response in patients with previously confirmed covid-19 disease. This enables our basic understanding of the immune response to covid-19, but this has clinical application by informing vaccination responses. If treatment with convalescent plasma is found effective in treatment COVID-19, antibody tests will also have a role in identifying suitable donors.
4) For seroprevalence surveys for research and public health monitoring.

In this article we will not discuss the latter two indications, but will focus on the benefits of antibody testing for individuals with and without symptoms suggestive of current or past covid-19 infection.

Accuracy of antibody tests

There are three main types of antibody produced in response to infection; IgA, IgG and IgM. IgM rises soonest and typically declines after infection, IgG and IgA persist and usually reflect longer term

immune response. Antibody tests include a variation of the above antibodies, either as separate or combined antibody measurement. Antibody tests can be done in laboratory settings using enzyme-linked immunosorbent assays (ELISA) or chemiluminescence immunoassays (CLIA) usually using venous blood samples. Point of care tests using disposable devices called lateral flow assays (LFAs) which use finger prick blood are also available. The main tests currently used in the NHS in the UK are the Abbott SARS-CoV-2 assay which detects IgG and the Roche Elecsys assay which detects both IgM and IgG. Both are CLIA assays which require venous blood. The accuracy of antibody tests is measured by comparing the test results to a 'gold standard', usually viral RNA detection by PCR testing at the time of symptoms. A limitation of this approach is the sensitivity in PCR testing. We do not yet have studies that measure outcomes such as rates of future Infection. Accuracy is therefore a measure of how well the tests detect previous covid-19 infections, not a direct measure of immunity to future infections.

A recent Cochrane review of covid-19 antibody testing included 57 publications on 54 cohort studies with 15,976 samples of which 8,526 were from cases of confirmed SARS-CoV-2 infection.[6] Measures of diagnostic accuracy varied depending on the timing of the tests (see **table 1**). The maximum sensitivity for combined IgG or IgM tests was 96% at days 22-35 post symptom onset. For IgG alone the maximum sensitivity was 88.2% at days 15-21 post symptom onset. Summary specificities were provided in 35 out of 54 studies and exceeded 98% for all types of antibody test. The authors warn that these estimates of accuracy must be interpreted with caution, as 89% of studies in the review were judged to be at high risk of bias. The potential consequence is that many of the tests are likely to be less sensitive than reported, meaning increased likelihood of false negatives. The majority only included patients who were diagnosed based on a positive RT-PCR test, which means that patients who have signs, symptoms and exposure to COVID-19 but negative PCR (who are defined in the China CDC and WHO case definitions as "probably COVID") are excluded. This is important as false

negative rates of PCR have been estimated between 2% and 29%[7]. Most studies recruited hospitalised patients often with severe symptoms who are likely to have a greater antibody response than those in community settings. None directly measured test accuracy in asymptomatic patients, who have been shown to have lower levels of IgG and greater reductions in antibody levels in the early convalescent phase.[8] Nearly all studies sampled covid-19 cases and non-cases separately; this methodology leads to bias and tends to over-estimate measures of accuracy.[9]

There was a lack of data on accuracy of tests beyond 35 days. The optimum time for covid-19 antibody testing based on current research appears to be 2-5 weeks post symptom onset. Tests performed after 5 weeks should be interpreted with caution, as there is some evidence to suggest antibody levels may wane,[10] which would be expected to decrease sensitivity of antibody tests and increase false negatives.

Interpreting antibody tests

Interpretation of test results depends not only on the accuracy of the test itself but also the pre-test probability of infection. This will vary significantly depending on the indication for testing; when screening asymptomatic individuals this will be relatively low, for those with suggestive symptoms it is likely to be much higher. We will illustrate this with two clinical cases.

Case 1

Anthony is 53 with a background of type 2 diabetes and a raised BMI. He works as a security guard in a shopping centre in Norwich. His wife is worried about his risk of exposure to covid-19 at work, and phones the GP surgery requesting an antibody test. He has not had any suggestive symptoms and has no known exposure, having been off work since the start of the pandemic.

Anthony's pre-test probability can be estimated based on the population covid-19 antibody seroprevalence in his area; in the East of England this is estimated to be around 10%.[11] As he has had

no symptoms or known exposure his probability of asymptomatic seroconversion is likely to be lower; for illustrative purposes we will estimate his pre-test probability at 5%.

We do not have any data on the accuracy of antibody assays in asymptomatic people to base our estimates on. We will start by using the average sensitivity of 91.4% and average specificity of 98.7% from the Cochrane review and consider what would change, if in all likelihood, the test had lower sensitivity. **Figure 1a** illustrates the outcomes of testing based on 1000 people like Anthony, with a pre-test probability of 5%. We would expect that 942 people would test negative, of whom 4 people (0.4%) would actually have had had covid-19 (false negatives). Considering that the test may well have lower sensitivity, particularly if the peak incidence and therefore likely time of infection is >35 days ago, this would proportionally increase the false negative rate. If the test made five times as many false negatives (sensitivity of 57%) then this would rise to 20 false negatives (2.1%) - still relatively low numbers due to the low prevalence. A negative test result would therefore mean Anthony is unlikely to have had covid-19 infection. However, of the 58 people who would test positive, 12 people (21%) would be falsely positive. This is important because a false positive could potentially influence Anthony's behaviour and adherence to infection control measures. This could be particularly risky as Anthony has an occupational risk of exposure and co-morbidities making him at higher risk of complications from covid-19. The GP should therefore explain that the test result cannot be used to indicate immunity, and that regardless of the results of testing Anthony should take precautions to avoid exposure to SARS-CoV-2. The test result in this case is therefore unlikely to change clinical management of the patient, and has the potential to cause harm through false reassurance.

Case 2

Sarah is 32 and has been unwell for 4 weeks with intermittent shortness of breath, myalgia, atypical chest pains, fatigue and anosmia. She never received a covid-19 swab test, as she did not have typical cough or fever symptoms. Her GP requests blood tests including covid-19 antibodies.

Sarah has prolonged symptoms which are in keeping with a possible diagnosis of coronavirus, although she has not had suffered the cardinal features of cough or fever. To try and clarify the underlying cause of Sarah's symptoms before embarking on further investigations, her GP requests blood tests including covid-19 antibodies. Her pre-test probability will be higher than Anthony, and will also depend on where she lives and whether she is known to have been exposed to the virus – for illustrative purposes we will estimate her pre-test probability of 50%. We will use the estimates of sensitivity and specificity for the test from the Cochrane review.[6]

Figure 1b shows the outcomes of testing based on 1000 people with a pre-test probability of 50%; 537 people would be expected to test negative, of whom 43 (8%) would have actually had covid-19 (false negatives). If the sensitivity was not as high as in the Cochrane review (which is likely because of the limitations of the primary studies that they mention) then number of false negatives would increase. This means a negative test in a patient like Sarah makes covid-19 less likely, but does not rule it out; Sarah might have had covid-19 but never developed an antibody response, her antibody levels could have dropped in the 4 weeks since symptom onset, or the test could have been unable to detect the antibodies which were present. However, the negative result would alert the clinician to consider other possible causes for Sarah's symptoms, which could help prevent missed or delayed diagnosis of other diseases in patients with symptoms assumed to be covid-19 related.

A positive test in this context would be much more compelling; of 1000 people tested, 464 people would test positive and only 7 (2%) would not have covid-19 (false positives). A positive test result in the context of suggestive symptoms therefore makes covid-19 infection highly probable. Antibody testing is therefore likely to be helpful in guiding clinical management of symptomatic patients like Sarah.

In summary, antibody tests have a high specificity, but sensitivity is variable and depends on time since symptom onset. Negative results should therefore be interpreted with caution in the context of typical symptoms. High specificity means false positives are rare (<2% of people who have not had

covid-19 will have a false positive test). However in low prevalence settings true positives are also rare, which means the predictive value of a positive test will be lower in individuals with a low background risk of infection. A positive result must therefore also be interpreted with caution in patients with a low pre-test probability, such as those with no history of suggestive symptoms or risk factors for exposure to SARS-CoV-2, as false positives could lead to false reassurance with potential for patient harms. This interactive calculator (https://www.bmj.com/content/369/bmj.m1808/article-info) allows clinicians to explore the impact of changing the pre-test probability, sensitivity and specificity on test outcomes. Residual uncertainty after diagnostic testing is normal, and the same principles apply to most screening and diagnostic tests. Covid-19 offers an opportunity to improve clinician and patient understanding and communication of risk and uncertainty in diagnostic testing. This raises a wider debate around testing and test evaluation for many diseases where the accuracy of tests has not been subject to this degree of scrutiny.

SARS-CoV-2 immunity

Antibodies are an essential component of the adaptive immune response providing specificity and memory against future infection. This is achieved through a number of mechanisms including neutralization by binding pathogens, activation of complement to destroy cells by lysis, presentation or opsonisation to immune cells to facilitate phagocytosis, degranulation and antibody dependent cell-mediated cytotoxicity.

However, for many viruses and intracellular infections such as tuberculosis, T cell immunity is predominant. There is an increasing literature on the role of T cells following SARS-CoV-2 infection.[12] T cell memory has now been demonstrated in laboratory tests, and cross reactivity of T cell responses to other coronavirus infections potentially explains some of the variation in clinical

severity of infection.[13] As for most intracellular infections, it is likely that a combination of B and T cell immunity is required for clearing covid-19 infection and generating protective memory.

Although we can test for the presence of antibodies, the extent to which SARS-CoV-2 antibodies provide future immunity and protection from repeat infection is not yet known. There is experimental evidence of neutralization with certain SARS-CoV-2 antibodies and inferred clinical evidence from very few reports of repeat infection and successful use of convalescent plasma therapy.[14 15] However, longitudinal studies are now reporting and showing that antibody levels are waning.[10] What we do not know is whether protective immunity will be maintained with a lower antibody titre.

To know whether our current antibody tests are indicative of protective immunity, ideally we would need disease prevalence studies in individuals with known antibody status, however knowing whether these antibodies are neutralizing in a laboratory should give us some indication before large population studies can be completed.

Lastly, antibodies have the ability to provide long term immunity but non neutralizing antibodies can also be produced and a phenomenon known as antibody enhancement can occur where antibodies facilitate a secondary infection that can be more severe than the primary infection.[17] This has been reported with other corona viruses but not to date with SARS-CoV-2.

Pitfalls of antibody testing

Testing policies that are population based and without a specific clinical indication, essentially amount to screening. This risks potential harm if the consequences of testing are not carefully considered. If testing is based on patient request, rather than clinically driven, we anticipate that there will be higher rates of testing in more affluent populations, who are at lower risk of covid-19, in keeping with the inverse care law.[18] This also limits the usefulness of data for estimates of seroprevalence, as a self-selecting population will not be representative. Concerns about the

implications of the rapid rollout of antibody testing have been raised[19] and the CMO in Scotland has advised against 'on-demand' testing.[20]

The Royal College of Pathologists has produced a covid-19 testing strategy, underpinned by seven principles, one of which is that *testing must be carried out for a purpose*.[21] It is arguable that doctors commonly use tests for the purposes of 'reassurance', [22] and this is therefore a justifiable rationale for testing. However two systematic reviews of randomised controlled trials found no evidence of effect of diagnostic tests on illness worry, non-specific anxiety or symptom persistence;[23 24] we do not know the effect of covid-19 testing on patient anxiety. There have been suggestions that the purpose of antibody testing should be to guide reopening of workplaces,[25] however until more is known about the relationship between antibodies and protective immunity results should not influence public health advice to individuals or workplaces. Even if future evidence demonstrates that antibodies do confer sufficient and lasting immunity, the concept of 'immunity passports' raises ethical issues, threatening freedom and fairness and potentially risking public health by incentivising people to wilfully seek out infection and antibody testing or encouraging a potential antibody testing black market.[26]

Public and political demand for testing should be balanced against the significant workload generated for laboratories doing the tests and GPs discussing implications before testing and results with patients. However if tests are not available through an NHS route, individuals may seek to access tests through private means where tests may not be as rigorously quality assured and individuals are less able to access the clinical interpretation of the result within the context of an individual's situation.

Conclusions

Antibody testing within rigorously designed and conducted seroprevalence studies is important for research and to guide public health interventions.[27] However clinicians should consider the risks and benefits of testing for individuals, and should carefully share information about the limitations of

testing with patients (**box 5**). High quality evidence on test accuracy is currently lacking, and further research is needed to address areas of uncertainty (**box 6**). For most asymptomatic individuals knowing their antibody status it is unlikely to change clinical management. A drive to increase volumes of tests performed without considering the clinical value of testing could be an expensive distraction from key public health interventions. Yet carefully considered testing, in patients with late presentation of the illness, prolonged or atypical symptoms could help reduce uncertainty, guide ongoing management and improve understanding of the late sequelae of covid-19.

Table 1: Sensitivity and specificity by time since symptom onset[6]

	Sensitivity					**Specificity**
	Days 1-7	Days 8-14	Days 15-21	Days 22-35	Days >35	All time points
IgG*	29.7% (22.1-38.6)	66.5% (57.9-74.2)	88.2% (83.5-91.8)	80.3% (72.4-86.4)	86.7% (79.6-91.7)	99.1% (98.3-99.6)
IgM	23.2% (14.9-34.2)	58.4% (45.5-70.3)	75.4% (64.3-83.8)	68.1% (55.0-78.9)	53.9% (38.4-68.6)	98.7% (97.4-99.3)
IgA	28.4% (0.9-94.3)	78.1% (9.5-99.2)	98.7% (39.0-100)	98.7% (91.9-99.8)	100% (85.2-100)	
IgG or IgM*	30.1% (21.4-40.7)	72.2% (63.5-79.5)	91.4% (87.0-94.4)	96.0% (90.6-98.3)	77.7% (66.0-86.2)	98.7% (97.2-99.4)

*The main tests currently used in the NHS in the UK are the Abbott SARS-CoV-2 assay which detects IgG and the Roche Elecsys assay which detects both IgM and IgG.

Box 2: Definitions

Sensitivity (*or true positive rate):* proportion of people who have had covid-19 who are correctly identified by a positive antibody test

Specificity *(or true negative rate*): proportion of people who have not had covid-19 who are correctly identified by a negative antibody test

True positives: people who have had covid-19 who have a positive test result

False positives: people who have not had covid-19 who have a positive test result

True negatives: people who have not had covid-19 who have a negative test result

False negatives: people who have had covid-19 who have a negative test result

For further reading on calculating measures of test accuracy see Loong et al[28]

Box 3: How patients were involved in the creation of this article

Two patient representatives from the University of Birmingham PPI panel reviewed this article. The feedback was that the article was interesting and readable, and the case studies were realistic. As a result of the feedback changes were made to the wording of box 5 'possible phrases to help explain antibody tests to patients'.

Box 4: How this article was made

This article was produced at speed to address an urgent need for evidence. JD has recently led a Cochrane systematic review of the diagnostic accuracy of covid-19 antibody tests and this paper is based on the evidence from this systematic review, with clinical input from JW and AR.

Box 5: Possible phrases to help explain covid-19 antibody tests to patients

- Antibody tests help us to find out who has had covid-19 in the past
- They cannot tell us for sure whether you can catch covid-19 in the future
- If the test is positive then it is likely that you have been infected at some time
- A negative test result cannot rule out the possibility that you have had covid-19.

Box 6: Uncertainties

- Most studies on antibody tests are from hospitalised patients – we do not know how well these tests work in patients with mild illness who were not hospitalised or asymptomatic patients
- There is a lack of data on test accuracy beyond 35 days – we do not know how well these tests will work for infections which occurred >5 weeks ago
- There is not enough evidence to know whether the presence of antibodies confers lasting immunity to protect against future covid-19 infection

Box 7: Education into practice

- What is the protocol for covid-19 antibody testing in your organisation?
- How do you explain covid-19 antibody test results to patients?
- Reflect on a recent case of covid-19 antibody testing – did the test results influence clinical management?

Author contributorship

JW AR and JD contributed to the conception of the work. JD has recently led a Cochrane systematic review of the diagnostic accuracy of covid-19 antibody tests and this paper is based on the evidence from this systematic review, with clinical input from JW and AR. JW wrote the first draft of the paper. JW, AR and JD all contributed to the revised drafts of the paper and approved the final version for submission.

Competing Interests

We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: AR is a collaborator from the University of Birmingham / Binding Site group developing assays for covid-19 antibody testing, JW and JD have no competing interests.

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Patient Consent

The cases in this article are fictitious and therefore no consent was needed.

References

1. Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. 2020;369:m1808. doi: 10.1136/bmj.m1808 %J BMJ
2. Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure.0(0):null. doi: 10.7326/m20-1495 %m 32422057
3. Mizumoto K, Kagaya K, Zarebski A, et al. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin* 2020;25(10) doi: 10.2807/1560-7917.Es.2020.25.10.2000180 [published Online First: 2020/03/19]
4. Petherick A. Developing antibody tests for SARS-CoV-2. *The Lancet* 2020;395(10230):1101-02. doi: 10.1016/S0140-6736(20)30788-1
5. Lind S. GPs to provide Covid antibody testing for patients who have bloods taken: Pulse; 2020 [Available from: http://www.pulsetoday.co.uk/news/gps-to-provide-covid-antibody-testing-for-patients-who-have-bloods-taken/20040894.article.
6. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database of Systematic Reviews* 2020(6) doi: 10.1002/14651858.CD013652
7. Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, et al. FALSE-NEGATIVE RESULTS OF INITIAL RT-PCR ASSAYS FOR COVID-19: A SYSTEMATIC REVIEW. 2020:2020.04.16.20066787. doi: 10.1101/2020.04.16.20066787 %J medRxiv
8. Long Q-X, Tang X-J, Shi Q-L, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nature Medicine* 2020 doi: 10.1038/s41591-020-0965-6
9. Whiting PF, Rutjes AWS, Westwood ME, et al. A systematic review classifies sources of bias and variation in diagnostic test accuracy studies. *Journal of clinical epidemiology* 2013;66(10):1093-104. doi: https://doi.org/10.1016/j.jclinepi.2013.05.014
10. Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19. 2020 doi: 10.1056/NEJMc2025179

11. England PH. Sero-surveillance of COVID-19 (updated 2 July 2020) 2020 [Available from: https://www.gov.uk/government/publications/national-covid-19-surveillance-reports/sero-surveillance-of-covid-19 accessed 07/07/2020.
12. Gallais F, Velay A, Wendling M-J, et al. Intrafamilial Exposure to SARS-CoV-2 Induces Cellular Immune Response without Seroconversion. 2020:2020.06.21.20132449. doi: 10.1101/2020.06.21.20132449 %J medRxiv
13. Le Bert N, Tan AT, Kunasegaran K, et al. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. *Nature* 2020 doi: 10.1038/s41586-020-2550-z
14. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. 2020;117(17):9490-96. doi: 10.1073/pnas.2004168117 %J Proceedings of the National Academy of Sciences
15. Wu F, Wang A, Liu M, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. 2020:2020.03.30.20047365. doi: 10.1101/2020.03.30.20047365 %J medRxiv
16. Lv H, Wu NC, Tsang OT-Y, et al. Cross-reactive antibody response between SARS-CoV-2 and SARS-CoV infections. 2020:2020.03.15.993097. doi: 10.1101/2020.03.15.993097 %J bioRxiv
17. Fierz W, Walz B. Antibody Dependent Enhancement Due to Original Antigenic Sin and the Development of SARS. *Front Immunol* 2020;11:1120-20. doi: 10.3389/fimmu.2020.01120
18. Tudor Hart J. THE INVERSE CARE LAW. *The Lancet* 1971;297(7696):405-12. doi: https://doi.org/10.1016/S0140-6736(71)92410-X
19. Andersson M, Low N, French N, et al. Rapid roll out of SARS-CoV-2 antibody testing—a concern. 2020;369:m2420. doi: 10.1136/bmj.m2420 %J BMJ
20. Government S. COVID-19 antibody testing 2020 [Available from: https://www.gov.scot/news/covid-19-antibody-testing-1/ accessed 07/07/2020.
21. Martin J. COVID-19 testing: a national strategy. *Royal College of Pathologists* 2020
22. Watson J, de Salis I, Banks J, et al. What do tests do for doctors? A qualitative study of blood testing in UK primary care. *Family Practice* 2017
23. Petrie KJ, Sherriff R. Normal diagnostic test results do not reassure patients. *Evidence-based medicine* 2013 doi: 10.1136/eb-2013-101393 [published Online First: 2013/07/13]
24. Rolfe A, Burton C. Reassurance after diagnostic testing with a low pretest probability of serious disease: Systematic review and meta-analysis. *JAMA internal medicine* 2013;173(6):407-16. doi: 10.1001/jamainternmed.2013.2762
25. Weinstein MC, Freedberg KA, Hyle EP, et al. Waiting for Certainty on Covid-19 Antibody Tests - At What Cost? *N Engl J Med* 2020 doi: 10.1056/NEJMp2017739 [published Online First: 2020/06/06]
26. Kofler N, Baylis F. Ten reasons why immunity passports are a bad idea. *Nature* 2020;581(7809):379-81. doi: 10.1038/d41586-020-01451-0 [published Online First: 2020/05/23]
27. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *The Lancet* doi: 10.1016/S0140-6736(20)31483-5
28. Loong T-W. Understanding sensitivity and specificity with the right side of the brain. 2003;327(7417):716-19. doi: 10.1136/bmj.327.7417.716 %J BMJ